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DISEASE OF THE PRIMARY MOTOR NEURONES CAUSING THE CLINICAL PICTURE OF ACUTE ANTERIOR POLIOMYELITIS: THE RESULT OF POISONING BY CYANIDE OF POTASSIUM

A CLINICAL AND EXPERIMENTAL CONTRIBUTION TO THE TOXIC
EFFECTS OF CYANIDE OF POTASSIUM UPON THE PERIPHERAL
MOTOR NEURONES ¹

BY JOSEPH COLLINS, M.D.,

ATTENDING PHYSICIAN TO THE NEW YORK CITY HOSPITAL,

AND HARRISON S. MARTLAND, M.D.,

RUSSELL SAGE INSTITUTE OF PATHOLOGY, CITY HOSPITAL

The peripheral motor neurones, that is, the ganglion cells in the anterior horns of the gray matter of the spinal cord and their processes, particularly the neuraxones or axis-cylinders, are susceptible to injury by many toxic and infectious agencies. When such agencies affect the cell-bodies or intra-spinal processes of the cell-bodies, the resulting disease is known as poliomyelitis. When the extra-spinal processes, or neuraxons, are diseased the condition is called neuritis. For a long time it was thought that the same agency which produces disease of the cell-body was not likely to produce disease of the neuraxone, and in a measure that belief is founded upon fact. The agencies that are most prone

¹ Read before the New York Neurological Society, March, 1908.

to cause inflammation of the motor nerves constituting motor neuritis, are probably not those responsible for inflammation or decay constituting poliomyelitis, save perhaps in very exceptional instances. Numerous investigators have shown that certain metallic substances, such as lead, cause degeneration of the motor nerves constituting a true motor neuritis. Such cases coming to autopsy have shown distinct degeneration of the anterior horn cells of the spinal cord. Moreover, it has been abundantly shown by many investigators, particularly by Stieglitz,¹ that experimental lead poisoning produces degeneration of the entire motor neurone. The question which awaits reply in those cases is the same as we shall raise in the present article, *i. e.*, which part of the primary motor neurone is first and principally affected in certain intoxications?

We have been unable to find any cases of neuritis or poliomyelitis produced by cyanide of potassium poisoning in a fairly careful search of the literature.² This article is offered as a contribution to that subject.

We report herewith a case of acute inflammation or degeneration of the peripheral motor neurones, which constitutes clinically a peripheral motor neuritis, but which, however, can scarcely be distinguished from an anterior poliomyelitis. In fact, so far as the reporters of the case are concerned, it cannot be distinguished.

The patient, an Italian, 38 years old, was admitted to the City Hospital, December 3, 1906. A brief synopsis of the history of his illness is as follows: Since coming to this country, in 1904, he had been working as a silver polisher in a hotel. The method of keeping silver bright in such establishments is to drop it into a solution of cyanide of potassium and then dry it. He says that his hands and forearms were in such solution so much of the time that they took on a deep brownish red color and he frequently complained of a distressing itching sensation in them. In addition to this the finger-nails were quite black. He does not know how strong the solution of cyanide of potassium was that he used, but he says that he had to be careful to keep his hands away from his nose or his mouth, for otherwise he would get very dizzy. On the seventh of September, 1906, he was

¹ Arch. f. Psych., Vol. 24, p. 1.

² Dr. Larkin, in discussing this paper said he had seen one instance of disease of the entire peripheral motor neurone following cyanide of potassium poisoning.

seized with diarrhea which soon became very severe, the passages containing large amounts of mucus but no blood. The following day he complained of severe headache, of pain and stiffness in the back of the neck and of feeling ill. He was then taken to a hospital and it is said that for a few days he was mildly delirious and had such meningeal symptoms as stiffness of the neck, retraction of the head and sensitiveness on being handled. These symptoms continued for four or five days. Then there developed a sensation of stiffness of both ankles and severe pain in the legs below the knees. Within forty-eight hours his legs and arms were so weak that he could scarcely move them, and from that time he was unable to stand or walk. About this time, *i. e.*, eight days after the onset of his symptoms, he had retention of urine and had to be catheterized for more than a week. After that he had difficulty in expelling the urine, but he got on without having a catheter passed. At this time he did not complain of pain or paresthesia, the symptoms were entirely of the motor apparatus, nor were there any trophic symptoms apparently. His best recollection concerning the atrophy of the muscles, which was so conspicuous on his entrance into the City Hospital, was that it was first noticed about eight weeks after the onset of his disease.

Examination at this time showed that the patient was bedridden, unable to move the lower extremities and to perform very few movements with the upper extremities. The atrophy of the muscles was the most conspicuous objective symptom, and the distribution of this atrophy was as follows: The trapezii were involved to a slight extent. The supra and infraspinati muscles, the serratus magnus, the deltoids, the biceps to a very considerable degree, and the triceps very conspicuously atrophied. The plantars and the extensors of the forearm were also very much shrunk. In the lower extremities the muscles chiefly involved were the anterior tibial group and the posterior calf muscles, the vasti and quadriceps. The left leg lies in a position of external rotation, and it is impossible for him to turn it inwards. Both feet are in a position of drop-foot, the right being more profoundly so than the left. The dorsal surfaces of the feet are slightly cyanotic; the nails show transverse ridges at their bases. The knee- and ankle-jerks are absent. There is a flexor plantar jerk. There is marked atrophy of the glutei over the left hip. In the upper extremities the left deltoid and the trapezius are atrophied and this atrophy throws the shoulder lower than on the opposite side. There is some atrophy of the muscles of both forearms, and there is marked shrinkage of the thenar and hypothenar eminences of the left hand.

Tactile, thermal and pain sensibility are normal. There is no disorder of function of any of the cranial nerves.

Electrical examination shows that the anterior tibial muscles contract on both sides with a strong faradic current. There is

a slight response to the faradic current in the quadriceps, but the reaction is sluggish and vermiform. In the other atrophied muscles the faradic contractility is lost apparently in proportion to the intensity of the atrophy. In all the muscles there is a slight reaction to the galvanic current with polar alteration characteristic of reaction of degeneration.

For upward of six months there seemed to be no indications of recovery. Then gradually the atrophied and paralyzed muscles of the upper extremity began to display slight functional capacity. In the autumn of 1907 braces were put upon his legs and now he is able to walk with the aid of crutches. Examination of him at the present time shows that the muscles of the neck and trunk are of good volume and capacity. Both deltoids are atrophied, the left more profoundly than the right. External rotation of the shoulders is weak. The muscles of the arm and forearm seem to be in good condition, save the supinator longus and the biceps of both sides. The triceps, which was very much affected in the beginning, now seems to be approximately normal. The extensors of the right wrist are weaker than those of the left, but there is no evidence of atrophy in the muscles. The cranial nerves are intact.

Flexion of the thighs is accomplished very indifferently, but better on the left side than on the right, while extension of the legs upon the thighs, which is also very weak, is accomplished better on the right than on the left. There is double foot-drop. He can flex the toes of the right foot but not of the left. The crural muscles and the calf muscles show the greatest amount of atrophy.

The knee-jerk is present on both sides but extremely weak and sluggish. The abdominal and cremasteric jerks are elicitable. The right Achilles jerk is present but sluggish, and the left absent. Tactile, pain, and thermal sensibility seems undisturbed. There is no tenderness of the nerves to deep-seated pressure. Distinct fibrillary movements are occasionally to be seen in the gluteal and deltoid muscles.

In other words, the patient has made a fairly good recovery and he is still improving. The only symptoms that tend to indicate the dependence of some of the atrophy upon spinal cord lesion is the fibrillary phenomenon to be observed in the muscles in which the atrophy is still most pronounced.

Taken in conjunction with the experimental work that has been done to determine the effect of cyanide of potassium upon the peripheral motor neurone, it is obvious that the entire motor neurone was affected by the poison but that the brunt of the lesion was borne by the axones at their periphery (see Plate I).

The important features of the disease as they presented themselves in this case were: (1) The rapidity with which the symp-

toms came on and their intensity. In character they were of an overwhelming intoxication or infection; (2) the occurrence of

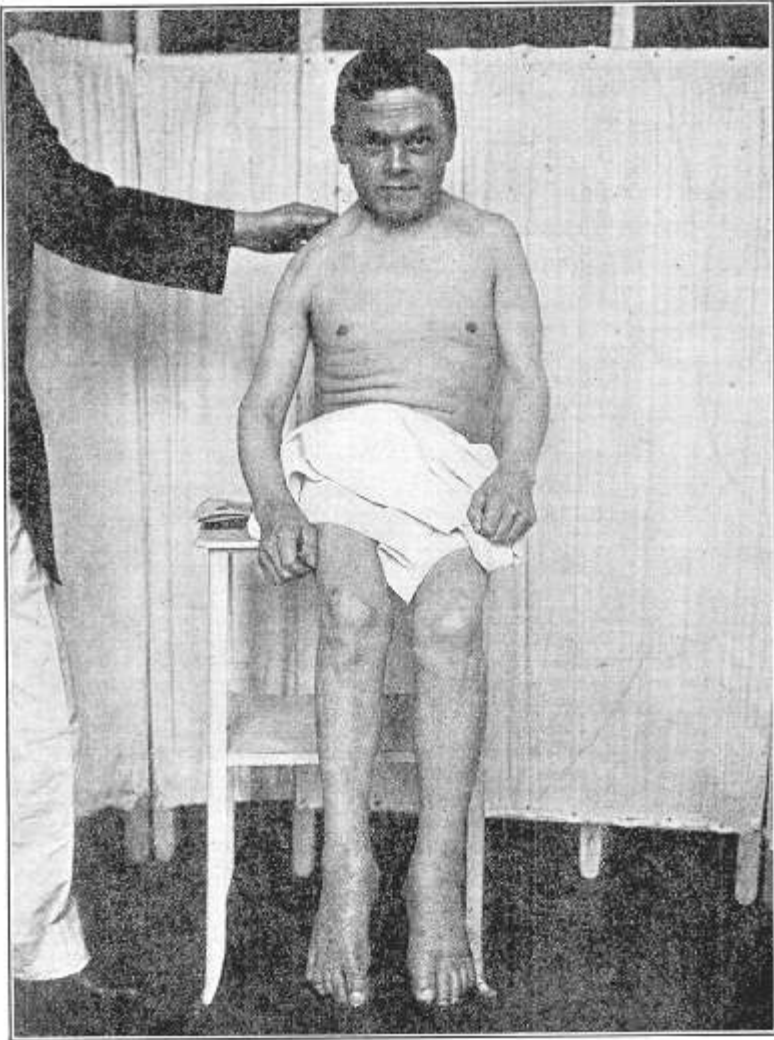


FIG. 1. Picture of patient showing drop foot atrophy, etc. spinal cord symptoms; (3) distribution of the atrophy and partial recovery.

Unlike the neuritis that is caused by other metallic poisons such as lead and arsenic, there seem to have been no premonitory

symptoms whatsoever, although there are cases of lead neuritis in which there has been no history of colic, digestive disturbances, etc., and there are cases of arsenical neuritis which are not preceded by the peculiar garlic odor of the breath; such cases are very uncommon. In our patient there seemed to have been no premonitory symptoms except the symptoms of gastro-intestinal irritation. The extent and intensity of the atrophy as well as the intensity of the motor incapacity which preceded it, bespeak the profound involvement of the motor neurones in their entirety.

From the experimental work which we have undertaken to show the effects of potassium cyanide upon the peripheral motor neurones, we are led to the belief that the entire motor neurone is affected, the neuraxone, however, more than the cell-body, but the participation of the cell-body in the destructive process is fairly certain, and this participation accounts for the occurrence of spinal cord symptoms in our patient. That the atrophy, however, that is, the degeneration in the muscles, is not primarily dependent upon spinal cord lesion, is best testified to by the distribution of the atrophy. It would have to be an extremely extensive process in the spinal cord and such extensive lesion would cause symptoms that did not occur in this case. Moreover, the degree of recovery which has taken place indicates that the cell-bodies of many of the peripheral motor neurones, which at first seemed to be very profoundly diseased because of the amount of atrophy, are in reality in possession of sufficient vitality to assist in the regeneration of the diseased neuraxons.

The following experiments were done for the purpose of studying the effects upon the nervous system of cyanide of potassium administered in poisonous doses:

Four healthy rabbits were used in the experiment. The two first died, the two last recovered.

The salt of hydrocyanic acid used was the potassium salt, which was made in a sterile water solution, 1 c.c. equaling 2 mg. of the pure salt. The injections were made with a sterile hypodermic syringe, usually into the posterior auricular vein. The wound was immediately sealed with collodion.

All spinal cord specimens were hardened in 10 per cent. formalin, followed by alcohol, imbedded in celloidin and cut at about 6 microns; sections were then stained in 1 per cent. aqueous methylenblue, being gently heated until the dye steamed; they were then differentiated in absolute alcohol, 90 parts, and anilin oil 10 parts, washed in alcohol and cleared in xylol.

Rabbit No. 1 received 2 mgs. of the drug every other day for a period of sixteen (16) days, or a total of 16 mgs. On the sixteenth day a complete flaccid paralysis of both hind legs was noticed, accompanied by loss of reflexes, and bladder and rectal incontinence. Sensation was apparently normal. On the seventeenth day the rabbit was much worse; both forefeet were now completely paralyzed, and there was slight twitching of the neck muscles. On the eighteenth day, as the animal lay in his cage, he was totally helpless, unable to hold up his head, and paid no attention when food was offered. Sudden disturbances, such as noise, were followed by convulsive movements of the head. Towards evening he died—sixty hours after the appearance of paralysis.

The following is a summary of the autopsy findings: Dilatation of the left ventricle of the heart; pulmonary edema, with hemorrhage in bronchi; parenchymatous degeneration of kidneys.

The following tabulates the distribution of the lesion found in the spinal cord: At the level of the oblongata, the anterior horn-cells were normal. Sections from the upper portion of the cervical enlargement were also normal; sections from the mid-portion of the cervical enlargement showed some neurones in various stages of degeneration. Sections from the mid-dorsal showed marked destruction of the anterior horn-cells of both horns. Sections from the lower dorsal also showed extreme destruction. Sections from the lumbar region showed scattered cells in various stages of destruction. Sections from the extreme lower lumbar region showed apparently normal neurones.

The changes observed in the anterior horn-cells were central chromatolysis with nuclear eccentricity, leading to entire destruction of cytoplasm, with vacuolization, shrinkage, and almost complete solution of the cell.

The lesion apparently commences in the chromatophilic granules which do not stain with the same intensity as they normally do; they appear pale and have ragged edges. At the same time, the nucleus also becomes swollen, and its nuclear membrane becomes well marked and distinct.

The chromatophile flakes now become granular and disintegrate, causing a great diminution in the number of bodies; this takes place first around the axone hill and nucleus. The cytoplasm around the nucleus becomes vacuolated, filled with fissures, or even entirely devoid of matter.

While the chromatolysis is going on, the nucleus also shows changes. Owing to a loss in substance of cytoplasm, it is left unsupported and falls to one edge of the cell—it becomes eccentric. The nucleoplasm becomes granular, causing the nuclear membrane to become puckered and crenated. The nucleolus remains clear and sharply defined, it being retained when all other structures of the cell are lost. The nuclear membrane is finally lost and complete destruction of the nucleus soon follows.

With such great loss in bulk of cell, it, as a whole, shrinks, leaving an open cell space; the cell may finally break up and disappear (see Plate II).

A portion of the right anterior tibial nerve, when teased out in glycerine and stained with osmic acid, showed extensive degeneration, with destruction of the myelin sheath, and the presence of irregular-sized fat droplets (see Plate III).

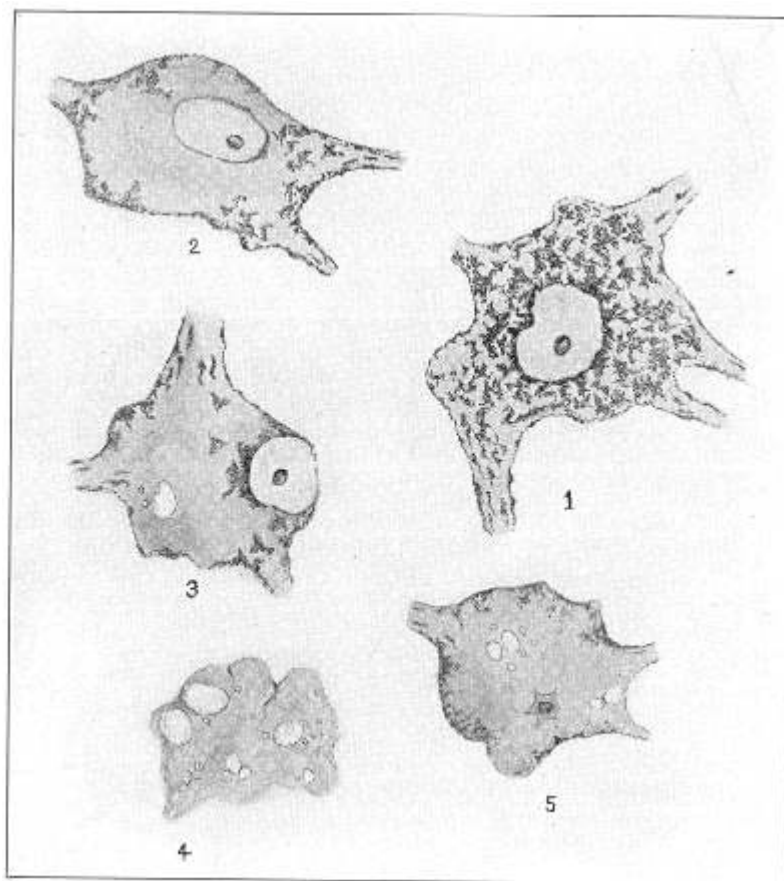


FIG. 2. Illustrating changes in ganglion cells of cord of rabbits.

Rabbit No. 2 received 2 mgs. every other day for ten days. At the end of this time the animal became very quiet, respirations and pulse were rapid, food was refused. On the morning of the next day the animal was paralyzed in both hind legs; at noon his forefeet were involved, and he died during the night—about twenty-four hours after paralysis had started.

The spinal cord was taken out immediately and studied, with the result that the anterior horn-cells, throughout the mid-cord, and in the cervical enlargement, showed the various stages of chromatolysis and neurone degeneration above described. Teased portions of the anterior tibial nerve showed fatty degeneration of myelin sheath.

Rabbit No. 3 received 12 mgs. over a period of fifteen days. Except for slight diarrhea he had no ill effects.

Rabbit No. 4 received as an initial dose 4 mgs. He immediately went into severe convulsions with rapid panting respirations, which soon stopped. Artificial respiration revived the ani-

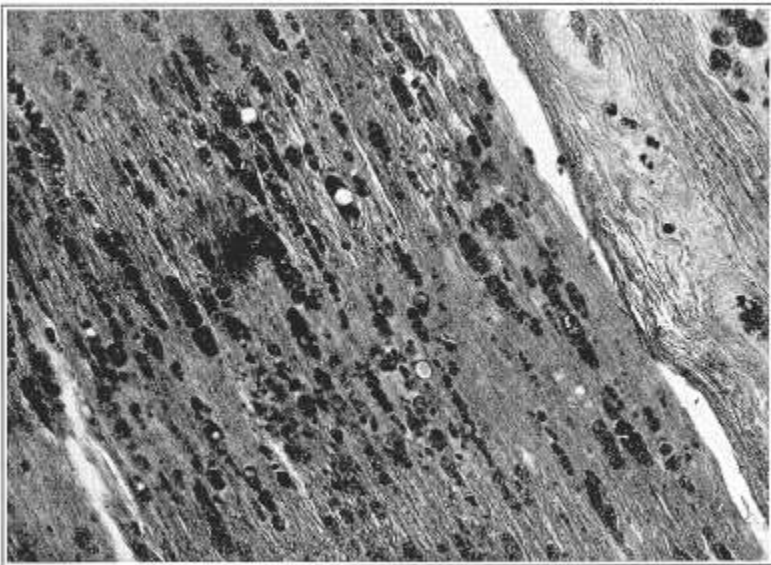


FIG. 3. Section of a peripheral nerve from a paralyzed rabbit, stained with osmic acid. Showing a severe parenchymatous neuritis, with formation of fat globules in the myelin sheath.

mal from the acute cyanide poisoning. After this he received a total of 14 mgs. in fourteen days, but no paralysis developed.

In the two last rabbits many of the injections were not made directly into the vein, but in the surrounding subcutaneous tissue.

There has been a great deal of controversy as to the nature of chromatophile bodies. F. B. Bailey (*Journal of Experimental Medicine*, 1901) concludes that "Nissl bodies are not present in the living cell, and that the chromatophile granules seen in the Nissl preparations represent a precipitation of the substance previously held in suspension in the cell protoplasm, caused by post-

mortem change, or action of fixatives." These bodies are best observed in tissues fixed in acid fixatives.

It is also not certain that the cytoreticulum is present in the living cell (as it can be seen only after fixation) or whether it, too, is a precipitate formed before, or at the time of the formation of the Nissl bodies.

These observations, however, make little difference in the case in question, as we know the chromatolysis (in our present conception of the term) is not the rule in the normal neurone and that a disappearance of the chromatophile bodies, as seen in these cases, associated with vacuolization and nuclear disintegration, is caused by a neurone injury, which leads to a partial or complete degeneration.

In conclusion, it would appear that the changes observed in the anterior horn-cells were due to a further extension of a peripheral multiple neuritis, that is, an axone degeneration which is so severe that it finally affects the neurone itself. In a chromatolysis, due to toxic material in the blood serum, which bathes the periphery of the cell, the chromatophile bodies are first destroyed around the periphery of the cell, and they last disappear around the nucleus, or, in other words, a peripheral chromatolysis is more common than a central one. A nuclear eccentricity is also very uncommon. In these cases, the foregoing, however, is not true. Here we have a chromatolysis which takes place, first, around the axone hill, and around the nucleus (a central chromatolysis), indicating that the cell has suffered internally, so to speak, by the extreme degeneration that has already taken place in its axone.